STIC-Biotech/ChemLib 59031

**From:** Chan, Christina
**Sent:** Friday, January 25, 2002 3:58 PM
**To:** Cook, Lisa; STIC-Biotech/ChemLib
**Subject:** RE: Rush Sequence Search

**Please rush. Thanks Chris**

CRF

-----Original Message-----
**From:** Cook, Lisa
**Sent:** Friday, January 25, 2002 3:51 PM
**To:** Chan, Christina
**Cc:** Chin, Chris
**Subject:** Rush Sequence Search

Chris,

Would you please approve.

Sequence search for seq. id. no. 3 in Application No. 09/582,711 (2 month amendment)
Claims 1-12: Peptide Epitopes Recognized by Antifilaggrin Autoantibodies in Serum from rheumatoid Arthritis Patients.
G. Serre et al.

Claims directed to a peptide comprising an epitope recognized by anti-flaggrin autoantibodies present in serum from rheumatoid arthritis patients, where
said epitope comprises the tripeptide motif Ser-Cit-His in which Cit represent a citrulline residue. Method and kits utilizing the peptide.

Claims also directed to an artificial antigen recognized specifically by anti-flaggrin autoantibodies present in serum from rheumatoid arthritis patients
comprising seq. id. no.3.

Thanks,

Lisa V. Cook
Patent Examiner
Art Unit 1641
703-305-0808

prot. 3

Searcher: D. Schneider
Phone: 308-4292
Location: CM1 12C14
Date Picked Up: 1/28
Date Completed: 1/31
Searcher Prep/Review: SGML Text 6
Clerical: _____
Online time: 5/20

TYPE OF SEARCH:
NA Sequences: 0
AA Sequences: 1
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST(where applic.)
STN: _____
DIALOG: 90,97
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: Compugen
WWW/Internet: _____
Other (specify): _____

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show files
File 155:MEDLINE(R) 1966-2002/Jan W1
File   5:Biosis Previews(R) 1969-2002/Jan W4
         (c) 2002 BIOSIS
File 315:ChemEng & Biotec Abs 1970-2002/Dec
         (c) 2002 DECHEMA
File  73:EMBASE 1974-2002/Jan W4
         (c) 2002 Elsevier Science B.V.
File 399:CA SEARCH(R) 1967-2002/UD=13605
         (c) 2002 AMERICAN CHEMICAL SOCIETY
File 351:Derwent WPI 1963-2001/UD,UM &UP=200207
         (c) 2002 Derwent Info Ltd
?ds

Set     Items   Description
S1       1609   FILAGGRIN? ? OR ANTI()FILAGGRIN? ? OR ANTIFILAGGRIN? ?
S2          8   FLAGGRIN? ? OR ANTI()FLAGGRIN? ? OR ANTIFLAGGRIN? ?
S3      11118   CITRULLIN?
S4    2010726   ANTIBOD? OR IMMUNOGLOBULIN? ?
S5     147579   RHEUMATOID()ARTHRITIS? ?
S6       1612   S1 OR S2
S7         69   S6 AND S3
S8         38   RD S7 (unique items)
S9      98156   AUTO()ANTIBOD? OR AUTOANTIBOD?
S10        29   S8 AND (S4 OR S9)
S11        24   S8 AND S5
S12        30   S11 OR S10
?t 12/7/all

 12/7/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12580353   21522063   PMID: 11665966
    Specific presence of intracellular citrullinated proteins in
 rheumatoid arthritis synovium: relevance to antifilaggrin
 autoantibodies .
  Baeten D; Peene I; Union A; Meheus L; Sebbag M; Serre G; Veys E M; De
Keyser F
  Department of Rheumatology, Ghent University Hospital, Belgium.
  Arthritis and rheumatism (United States) Oct 2001, 44 (10) p2255-62,
ISSN 0004-3591   Journal Code: 0370605
  Comment in Arthritis Rheum. 2001 Oct;44(10) 2218-20; Comment in PMID
11665960
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  OBJECTIVE: To investigate the presence of citrullinated proteins in the
synovial membrane of patients with rheumatoid arthritis (RA) and
controls, and to analyze a possible relationship with antifilaggrin
 autoantibody (AFA) reactivity. METHODS: Synovial biopsy samples were
obtained from 88 consecutive patients undergoing needle arthroscopy for
knee synovitis associated with RA (n = 36), spondylarthropathy (n = 35),
osteoarthritis (n = 9), or other diagnoses (n = 8). Tissue sections were
stained with 2 different anticitrulline polyclonal antibodies and an
 antifilaggrin monoclonal antibody (mAb). The phenotype of citrulline
-positive cells and the colocalization with affinity-purified AFA were
investigated by double immunofluorescence on frozen sections. RESULTS:
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Studies with the first antibody showed that citrulline is expressed intracellularly in the lining and sublining layers of RA synovial tissue. Staining with the second antibody , monospecific for proteins containing modified citrulline , and with anti-inducible nitric oxide synthetase confirmed the presence of citrullinated proteins rather than free citrulline in the synovium. Citrulline -positive cells were detected in 50% of the RA patients (18 of 36) but in none of the controls (0 of 52). The anticitrulline reactivity colocalized with affinity-purified AFA reactivity, although stainings with the antifilaggrin mAb indicated the absence of filaggrin in the synovium. CONCLUSION: Intracellular citrullinated proteins, which are not recognized by an antifilaggrin mAb, are expressed in RA but not in control synovium. The high specificity of this finding and the colocalization with AFA reactivity boost the interest in citrullinated proteins as possible triggers of autoimmune responses in RA. Moreover, this is the first description of a specific histologic marker for RA synovium.

Record Date Created: 20011022

12/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11686527 21393638 PMID: 11502616

Performance of two ELISAs for antifilaggrin autoantibodies , using either affinity purified or deiminated recombinant human filaggrin , in the diagnosis of rheumatoid arthritis .

Nogueira L; Sebbag M; Vincent C; Arnaud M; Fournie B; Cantagrel A; Jolivet M; Serre G

Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale (CJF 96-02), Toulouse-Purpan School of Medicine, University of Toulouse III (IFR Claude de Preval, INSERM-CNRS-UPS - CHU), France.

Annals of the rheumatic diseases (England) Sep 2001, 60 (9) p882-7, ISSN 0003-4967 Journal Code: 62W

Languages: ENGLISH

Document type: Journal Article; Validation Studies

Record type: Completed

OBJECTIVE: To develop a standardisable enzyme linked immunosorbent assay (ELISA), using human filaggrin , for detection of antifilaggrin autoantibodies in rheumatoid arthritis (RA). To compare the diagnostic performance of the ELISA with those of reference tests: "antikeratin antibodies " ("AKA"), and antibodies to human epidermis filaggrin detected by immunoblotting (AhFA-IB). METHODS: Two ELISAs were developed using either affinity purified neutral-acidic human epidermis filaggrin (AhFA-ELISA-pur) or a recombinant human filaggrin deiminated in vitro (AhFA-ELISA-rec) as immunosorbent. Antifilaggrin autoantibodies were assayed in 714 serum samples from patients with well characterised rheumatic diseases, including 241 RA and 473 other rheumatic diseases, using the two ELISAs. "AKA" and AhFA-IB tests were carried out in the same series of patients. The diagnostic performance of the four tests was compared and their relationships analysed. RESULTS: The titres of "AKA", AhFA-IB, and the AhFA-ELISAs correlated strongly with each other. The diagnostic sensitivity of the AhFA-ELISA-rec, which was better than that of AhFA-ELISA-pur, was 0.52 for a specificity of 0.95. This performance was similar to those of "AKA" or AhFA-IB. However, combining AhFA-ELISA-rec with AhFA-IB led to a diagnostic sensitivity of 0.55 for a specificity of 0.99. CONCLUSION: A simple and easily standardisable ELISA for detection of

antifilaggrin autoantibodies was developed and validated on a large series of patients using a citrullinated recombinant human filaggrin . The diagnostic performance of the test was similar to that of the "AKA" and AhFA-IB. Nevertheless, combining the AhFA-ELISA-rec with one of the other tests clearly enhanced the performance.
Record Date Created: 20010814

12/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11280225 21136399 PMID: 11238669
The major synovial targets of the rheumatoid arthritis -specific antifilaggrin autoantibodies are deiminated forms of the alpha- and beta-chains of fibrin.
Masson-Bessiere C; Sebbag M; Girbal-Neuhauser E; Nogueira L; Vincent C; Senshu T; Serre G
Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale Contrat Jeune Formation 96-02, Toulouse-Purpan School of Medicine, University Toulouse III, Toulouse, France.
Journal of immunology (United States) Mar 15 2001, 166 (6) p4177-84, ISSN 0022-1767 Journal Code: IFB
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
IgG antifilaggrin autoantibodies (AFA) are the most specific serological markers of rheumatoid arthritis . In epithelial tissues, they recognize citrulline -bearing epitopes present on various molecular forms of (pro) filaggrin . Histological analysis of rheumatoid synovial membranes with an Ab to citrulline showed labeling of interstitial amorphous deposits and mononuclear cells of various types. Immunochemical analysis of exhaustive sequential extracts of the same tissues showed that they contain several deiminated ( citrulline containing) proteins. Among them, two proteins, p64--78 and p55--61, present in urea-DTT and guanidine extracts, were shown by immunoblotting to be specifically targeted by AFA. By amino-terminal sequencing the proteins were identified as deiminated forms of the alpha- and beta-chains of fibrin, respectively. Their identity was confirmed using several Abs specific for the A alpha- and/or to the B beta-chain of fibrin(ogen). Moreover, AFA-positive rheumatoid arthritis (RA) sera and purified AFA were highly reactive to the A alpha- and B beta-chains of human fibrinogen only after deimination of the molecules by a peptidylarginine deiminase. Autoantibodies affinity purified from a pool of RA sera onto deiminated fibrinogen were reactive toward all of the epithelial and synovial targets of AFA. This confirmed that the autoantibodies to the deiminated A alpha-and B beta-chains of fibrinogen, the autoantibodies to the synovial proteins p64--78 and p55--61, and, lastly, AFA, constitute largely overlapping autoantibody populations. These results show that deiminated forms of fibrin deposited in the rheumatoid synovial membranes are the major target of AFA. They suggest that autoimmunization against deiminated fibrin is a critical step in RA pathogenesis.
Record Date Created: 20010312

12/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11001109 21062417 PMID: 11056669
Rheumatoid arthritis associated autoantibodies in patients with synovitis of recent onset.
Goldbach-Mansky R; Lee J; McCoy A; Hoxworth J; Yarboro C; Smolen JS; Steiner G; Rosen A; Zhang C; Menard HA; Zhou ZJ; Palosuo T; Van Venrooij WJ ; Wilder RL; Klippel JH; Schumacher HR; EI-Gabalawy HS
Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskelatal and Skin Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.
Arthritis research (England) 2000, 2 (3) p236-43, ISSN 1465-9905 Journal Code: DWZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
STATEMENT OF FINDINGS: An inception cohort of 238 patients having peripheral joint synovitis of less than 12 months duration was evaluated clinically and followed prospectively for 1 year to determine the clinical significance of a number of rheumatoid arthritis (RA) associated autoantibodies . Serum samples collected at the time of the initial evaluation were tested for rheumatoid factor (RF) and antibodies to Sa (anti-Sa), RA-33, (pro) filaggrin [ antifilaggrin antibody (AFA)], cyclic citrullinated peptide (anti-CCP), calpastatin, and keratin [antikeratin antibody (AKA)]. RF had a sensitivity of 66% and a specificity of 87% for RA. Anti-Sa, AFA, and anti-CCP all had a specificity of more than 90%, but a sensitivity of less than 50% for this diagnosis. Overall, there was a high degree of correlation between AFA, AKA, anti-Sa or anti-CCP, this being highest between anti-Sa and anti-CCP (odds ratio, 13.3; $P < 0.001$). Of the 101 patients who were positive for at least one of these four autoantibodies , 57% were positive for only one. Finally, anti-SA identified a subset of predominantly male RA patients with severe, erosive disease. Anti-SA, AFA and anti-CCP are all specific for early RA but, overall, have little additional diagnostic value over RF alone. Although these antibodies may preferentially recognize citrullinated antigens, the modest degree of concordance between them in individual patient sera suggests that it is unlikely a single antigen is involved in generating these responses.
Record Date Created: 20010126

12/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10958924 21019536 PMID: 11138614
Progress in the use of biochemical and biological markers for evaluation of rheumatoid arthritis .
Nakamura RM
Department of Pathology, Scripps Clinic, La Jolla, California 92037, USA.
Journal of clinical laboratory analysis (United States) 2000, 14 (6) p305-13, ISSN 0887-8013 Journal Code: JLA
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Rheumatoid arthritis (RA) is a chronic systemic inflammatory autoimmune disorder which is predominant in females. The exact etiology remains undefined. Recently, a large number of biochemical and biologic markers, which are useful in the diagnosis, prognosis, and monitoring

therapy of RA, have been reported. The new markers include genetic markers, filaggrin , citrulline containing peptides, A2/RA33, cytokines, joint and collagen breakdown products, and bone turnover markers. No laboratory tests in and of themselves are diagnostic of RA. The new markers have been employed in monitoring RA patients during treatment and following the course of the disease. With the development of innovative therapies for RA, many of the biochemical and biologic markers will be useful. (80 Refs.)
Record Date Created: 20010102

12/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10885131 20532587 PMID: 11069618
Human peptidylarginine deiminase type III: molecular cloning and nucleotide sequence of the cDNA, properties of the recombinant enzyme, and immunohistochemical localization in human skin.
Kanno T; Kawada A; Yamanouchi J; Yosida-Noro C; Yoshiki A; Shiraiwa M; Kusakabe M; Manabe M; Tezuka T; Takahara H
Department of Applied Biological Resource Science, School of Agriculture, Ibaraki University, Ami-machi, Inashiki-gun, Ibaraki, Japan; Department of Dermatology, School of Medicine, Kinki University, Oonohigashi, Osakasayama-shi, Osak.
Journal of investigative dermatology (UNITED STATES) Nov 2000, 115 (5) p813-23, ISSN 0022-202X Journal Code: IHZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Peptidylarginine deiminase catalyzes the post-translational modification of proteins through the conversion of arginine to citrulline in the presence of calcium ions. In rodents, peptidylarginine deiminase has been classified into four isoforms, types I, II, III, and IV, which are distinct in their molecular weights, substrate specificities, and tissue localization. Of these isoforms, only type III was detected in epidermis and hair follicles. Although the role of this enzyme in these tissues is not yet clear, indirect data have shown that several structural proteins such as filaggrin , trichohyalin, and keratin are substrates for peptidylarginine deiminase. In this study, we cloned the full-length cDNA of human peptidylarginine deiminase type III (3142 bp) from cultured human keratinocytes by reverse transcription-polymerase chain reaction and by rapid amplification of cDNA ends methods. This cDNA contained a 1995 bp open reading frame encoding 664 amino acids (Mr = 74 770). To explore the physicochemical and enzymatic properties of human peptidylarginine deiminase type III, we constructed a plasmid for producing a recombinant human peptidylarginine deiminase type III in bacteria. The enzymatic characteristics of the recombinant enzyme were very similar to those of the rodent peptidylarginine deiminase type III. The recombinant enzyme showed the catalytic activities toward structural proteins of epidermis and hair follicle, filaggrin and trichohyalin, in which the deiminations maxima of about 60% and 13% arginine residues were observed in filaggrin and trichohyalin, respectively. An immunohistochemical study of human scalp skin with a monospecific anti-peptidyl-arginine deiminase type III antibody revealed that the type III enzyme was localized to the inner root sheath and outer root sheath of hair follicles. Peptidylarginine deiminase type III in the inner root sheath was notable between supramatrix and keratogenous zone and was scarcely detected in cornified hair zone. The enzyme was also expressed in the cuticle layer of hair. On the other hand,

expression of the enzyme in the epidermis was very low. These data imply that human peptidylarginine deiminase type III is the predominant isoform in hair follicles and may function as a modulator of hair structural proteins, including trichohyalin during hair and hair follicle formation.
Record Date Created: 20001206

12/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09988840 99101527 PMID: 9886436
The epitopes targeted by the rheumatoid arthritis -associated antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro) filaggrin by deimination of arginine residues.
Girbal-Neuhauser E; Durieux JJ; Arnaud M; Dalbon P; Sebbag M; Vincent C; Simon M; Senshu T; Masson-Bessiere C; Jolivet-Reynaud C; Jolivet M; Serre G
Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale, Toulouse-Purpan School of Medicine, University Toulouse III, France.
Journal of immunology (UNITED STATES) Jan 1 1999, 162 (1) p585-94, ISSN 0022-1767 Journal Code: IFB
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies associated to rheumatoid arthritis (RA), which includes the so-called "antikeratin" Abs and antiperinuclear factor. AFA are the most specific serological markers of RA. We previously showed that they recognize human epidermal filaggrin and other profilaggrin-related proteins of various epithelial tissues. Here, we report further characterization of the protein Ags and epitopes targeted by AFA. All the Ags that exhibit numerous neutral/ acidic isoelectric variants were immunochemically demonstrated to be deiminated proteins. In vitro deimination of a recombinant human filaggrin by a peptidylarginine deiminase generated AFA epitopes on the protein. Moreover, two of three filaggrin -derived synthetic peptides with a citrulline in the central position were specifically and widely recognized by AFA affinity-purified from a series of RA sera. These results indicate that citrulline residues are constitutive of the AFA epitopes, but only in the context of specific amino acid sequences of filaggrin . In competition experiments, the two peptides abolished the AFA reactivity of RA sera, showing that they present major AFA epitopes. These data should help in the identification of a putative deiminated AFA-inducing or cross-reactive articular autoantigen and provide new insights into the pathogenesis of RA. They could also open the way toward specific immunosuppressive and/or preventive therapy of RA.
Record Date Created: 19990121

12/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09917790 98449902 PMID: 9774629
Deimination of 70-kD nuclear protein during epidermal apoptotic events in vitro.
Mizoguchi M; Manabe M; Kawamura Y; Kondo Y; Ishidoh K; Kominami E; Watanabe K; Asaga H; Senshu T; Ogawa H
Department of Dermatology, Tokyo Metropolitan Institute of Gerontology,

Tokyo, Japan.
journal of histochemistry and cytochemistry (UNITED STATES) Nov 1998, 46 (11) p1303-9, ISSN 0022-1554 Journal Code: IDZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Peptidylarginine deiminase (PAD) is the enzyme responsible for converting protein-bound arginine residues to citrulline . It has recently been shown that a number of epidermal proteins, including filaggrin , trichohyalin, and keratins, are deiminated by the action of PAD, suggesting a possible role for protein deimination during the final stages of epidermal differentiation. We report here a novel PAD substrate found during the course of identifying deiminated proteins in cultured rat epidermal keratinocytes. We found that a 70-kD protein localized to the periphery of the nucleus was preferentially deiminated after ionomycin treatment in the presence of 2 mM calcium and was associated with apoptotic events in these cells. Furthermore, we discovered that the deimination of nuclear protein could be induced by transfection of a PAD cDNA into rat epidermal keratinocytes. These data suggest that PAD may act on the 70-kD nuclear protein to induce disassembly of the nuclear lamina and promote apoptosis during terminal epidermal differentiation.

Record Date Created: 19981103

12/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09806570 98271249 PMID: 9608322
Are autoantibodies active players or epiphenomena?
Smolen JS; Steiner G
Department of Internal Medicine III, Allgemeines Krankenhaus, Waehringer Guertel, Wien, Austria.
Current opinion in rheumatology (UNITED STATES) May 1998, 10 (3) p201-6, ISSN 1040-8711 Journal Code: AVG
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed

Autoantibodies have the potential of pathogenicity in several diseases. In rheumatoid arthritis (RA), however, this has not been ultimately proven. RA is characterized by a variety of autoantibodies . Newer insights into characteristics of rheumatoid factors indirectly suggest their pathogenetic involvement. In contrast, antibodies to collagen, despite the availability of an experimental model, do not appear to be pathogenetic in man. Anti-hnRNP antibodies , particularly anti-A2/RA33, are present in RA and experimental models of RA, and therefore, aside from their diagnostic value in established and early RA, could also be involved in the disease process. The nature of Sa, another target antigen in RA, has not yet been elucidated. Filaggrin is the antigen recognized by antikeratin antibodies and antiperinuclear factor; however, citrullin is the target amino acid in filaggrin , and anticitrullin antibodies have a high predictive value. Among a series of cartilage proteins, most have not yet been characterized sufficiently; one, gp39, appears to be of particular interest. Whether or not these antibodies are involved in RA pathogenesis is not yet known. It can be speculated that autoimmunity to some, if not all, of these autoantigens mirrors events important in the development of RA, but further studies on T-cell reactivities and in experimental models are needed to fully understand the involvement. (62

Refs.)
Record Date Created: 19980803

12/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09639609 98083149 PMID: 9421490
Citrulline is an essential constituent of antigenic determinants recognized by rheumatoid arthritis -specific autoantibodies .
Schellekens GA; de Jong BA; van den Hoogen FH; van de Putte LB; van Venrooij WJ
Department of Biochemistry, University of Nijmegen, 6500 HB Nijmegen, The Netherlands. g.schellekens@bioch.kun.nl
Journal of clinical investigation (UNITED STATES) Jan 1 1998, 101 (1) p273-81, ISSN 0021-9738 Journal Code: HS7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Only a few autoantibodies that are more or less specific for RA have been described so far. The rheumatoid factor most often tested for is not very specific for RA, while the more specific antiperinuclear factor for several reasons is not routinely used as a serological parameter. Here we show that autoantibodies reactive with synthetic peptides containing the unusual amino acid citrulline , a posttranslationally modified arginine residue, are specifically present in the sera of RA patients. Using several citrulline -containing peptide variants in ELISA, antibodies could be detected in 76% of RA sera with a specificity of 96%. Sera showed a remarkable variety in the reactivity pattern towards different citrulline -containing peptides. Affinity-purified antibodies were shown to be positive in the immunofluorescence-based antiperinuclear factor test, and in the so-called antikeratin antibody test, and were reactive towards filaggrin extracted from human epidermis. The specific nature of these antibodies and the presence of these antibodies early in disease, even before other disease manifestations occur, are indicative for a possible role of citrulline -containing epitopes in the pathogenesis of RA.
Record Date Created: 19980209

12/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08590329 95363223 PMID: 7543546
Detection of deiminated proteins in rat skin: probing with a monospecific antibody after modification of citrulline residues.
Senshu T; Akiyama K; Kan S; Asaga H; Ishigami A; Manabe M
Department of Cell Chemistry, Tokyo Metropolitan Institute of Gerontology, Japan.
Journal of investigative dermatology (UNITED STATES) Aug 1995, 105 (2) p163-9, ISSN 0022-202X Journal Code: IHZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We performed a systematic study on deiminated proteins present in rat epidermis. Proteins extracted from various epidermal samples were resolved by either one- or two-dimensional gel electrophoresis and Western blotted to nitrocellulose membranes. Deiminated proteins were detected by

modification of citrulline residues followed by probing with an anti-modified citrulline monospecific antibody . The cornified layer of adult plantar skin gave multiple series of isoelectric variants, most of which were found to be differentially deiminated type II keratins (60 kDa, and 67 kDa or above). The whole epidermis of 5-day-old rat back skin showed isoelectric variants of 60-kDa keratin as major deiminated components, and deiminated 55-kDa keratin and deiminated filaggrin as minor spots. In addition, we found highly deiminated proteins (200-220 kDa) thought to be derived from trichohyalin. The immunoreactivity of deiminated proteins was mainly localized in the granular and cornified layers of epidermis. Co-localization of deiminated filaggrin and keratins in the granular layer suggests the possible role of protein deimination during the terminal stage of epidermal differentiation.
Record Date Created: 19950912

12/7/12 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)


13330219 BIOSIS NO.: 200100537368
HLA DR shared epitope, rheumatoid factor, anti-perinuclear factor, antifilaggrin and anti-cyclic citrullinated peptide antibodies in patients with longstanding rheumatoid arthritis : Relation with radiological progression.
AUTHOR: Peene I(a); Kruithof E(a); Union A; Meheus L; Mielants H(a); Veys E M(a); De Keyser F(a)
AUTHOR ADDRESS: (a)Dept. of Rheumatology, Ghent University Hospital, Ghent **Belgium
JOURNAL: Clinical Rheumatology 20 (5):p397 2001
MEDIUM: print
CONFERENCE/MEETING: 5th Belgian Congress on Rheumatology Hasselt, Belgium September 27-29, 2001
ISSN: 0770-3198
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

12/7/13 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)


13324173 BIOSIS NO.: 200100531322
Studying the role of the citrullin -containing epitopes of filaggrin in rheumatoid arthritis .
AUTHOR: Magyar A(a); Brozik M; Tobi R(a); Szabo T(a); Szakonyi J; Rojkovich B; Gergely P; Hudecz F(a)
AUTHOR ADDRESS: (a)Research Group of Peptide Chemistry Hungarian Academy of Science, Budapest**Hungary
JOURNAL: Amino Acids (Vienna) 21 (1):p24 2001
MEDIUM: print
CONFERENCE/MEETING: 7th International Congress on Amino Acids and Proteins Vienna, Austria August 06-10, 2001
ISSN: 0939-4451
RECORD TYPE: Citation
LANGUAGE: English

SUMMARY LANGUAGE: English

12/7/14 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)


11686962 BIOSIS NO.: 199800468693
Epitope mapping of natural filaggrin leads to the identification of rheumatoid arthritis -immunoreactive epitopes containing citrulline .
AUTHOR: Union Ann(a); Amerijckx Liesbet(a); Raymackers Jos(a); Dauwe Martine(a); De Keyser Filip; Veys Eric; Meheus Lydie(a)
AUTHOR ADDRESS: (a)Innogenetics N.V., Industriepark 7, 9052 Ghent**Belgium
JOURNAL: Arthritis & Rheumatism 41 (9 SUPPL.):pS84 Sept., 1998
CONFERENCE/MEETING: 62nd National Scientific Meeting of the American College of Rheumatology and the 33rd National Scientific Meeting of the Association of Rheumatology Health Professionals San Diego, California, USA November 8-12, 1998
SPONSOR: American College of Rheumatology
ISSN: 0004-3591
RECORD TYPE: Citation
LANGUAGE: English

RC927.A1 A7

12/7/15 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)


11377066 BIOSIS NO.: 199800158398
The modified arginine residue citrulline is the major constituent of epitopes recognized by autoantibodies in sera from rheumatoid arthritis patients.
AUTHOR: Schellekens G A(a); De Jong B A W(a); Van Den Hoogen F H J; Van De Putte L B A; Van Venrooij W J(a)
AUTHOR ADDRESS: (a)Dep. Biochem., Univ. Nijmegen, Nijmegen**Netherlands
JOURNAL: Arthritis & Rheumatism 40 (9 SUPPL.):pS276 Sept., 1997
CONFERENCE/MEETING: 61st National Scientific Meeting of the American College of Rheumatology and the 32nd National Scientific Meeting of the Association of Rheumatology Health Professionals Washington, DC, USA November 8-12, 1997
SPONSOR: Association of Rheumatology Health Professionals
ISSN: 0004-3591
RECORD TYPE: Citation
LANGUAGE: English

12/7/16 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE


11244719 EMBASE No: 2001259377
Chicken and egg in autoimmunity and joint inflammation
Burkhardt H.; Kalden J.R.; Schulze-Koops H.
H. Burkhardt, University of Erlangen-Nuremberg, Dept. of Internal Medicine III, Institute for Clinical Immunology, Krankenhausstrasse 12, 91054 Erlangen Germany
AUTHOR EMAIL: Harald.Bukhardt@med3.imed.uni-erlangen.de

Trends in Immunology ( TRENDS IMMUNOL. ) (United Kingdom) 2001, 22/6 (291-293)
CODEN: TIRMA ISSN: 1471-4906
PUBLISHER ITEM IDENTIFIER: S1471490601019354
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 5

12/7/17 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE


11089432 EMBASE No: 2001107067
Insights into rheumatoid arthritis derived from the Sa immune system
Menard H.A.; Lapointe E.; Rochdi M.D.; Zhou Z.J.
H.A. Menard, McGill University Health Center, Montreal General Hospital, Division of Rheumatology, 1650 Cedar Avenue, Montreal, Que. H3G 1A4 Canada
AUTHOR EMAIL: henri.a.menard@muhc.mcgill.ca
Arthritis Research ( ARTHRITIS RES. ) (United Kingdom) 2000, 2/6 (429-432)
CODEN: ARREC ISSN: 1465-9905
DOCUMENT TYPE: Journal ; Note
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 31

The Sa system is a recently described immune system that has a specificity and positive predictive value of nearly 100% for rheumatoid arthritis (RA) in Asia, Europe and the Americas. Its sensitivity of 30-40% suggests that it identifies a subset of RA patients. Anti-Sa antibodies are present from disease onset and are predictive of disease severity. The immune reactants are plentiful in the target tissue: antigen is present in the synovium, IgG antibody in the fluid. Immunologically, Sa is a hapten-carrier antigen in which vimentin is the carrier and citrulline is the hapten. The citrullination of vimentin is closely related to apoptosis, and citrullinated vimentin is extremely sensitive to digestion by the ubiquitous calpains. Nevertheless, Sa is found in only a few cell lines. Calpastatin, the natural specific inhibitor of calpains, is also a RA-associated, albeit non-specific, autoimmune system. Is it possible that calpain-related apoptotic pathways could be prominent in cells containing Sa? The task is to reconcile the specificity of Sa/ citrullinated proteins in a multifactorial and polygenic disease such as RA.

12/7/18 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE


11089391 EMBASE No: 2001107026
Citrullination : A small change for a protein with great consequences for rheumatoid arthritis
van Venrooij W.J.; Pruijn G.J.M.
W.J. van Venrooij, Department of Biochemistry, University of Nijmegen, PO Box 9101, Nijmegen HB-6500 Netherlands
AUTHOR EMAIL: W.vanVenrooij@bioch.kun.nl
Arthritis Research ( ARTHRITIS RES. ) (United Kingdom) 2000, 2/4

(249-251)
CODEN: ARREC ISSN: 1465-9905
DOCUMENT TYPE: Journal ; Note
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 20

A new autoantibody activity, which is almost 100% specific for rheumatoid arthritis (RA), has been found. The essential part of the B-cell epitope is a modified form of arginine (ie citrulline ). The conversion of protein-contained arginine to citrulline is an enzymatic process that is carried out by peptidylarginine deiminase (PAD), an enzyme that appears to be hormonally controlled. Because of its remarkable specificity, citrullination and related processes might open new possibilities for studying the aetiology of RA.

12/7/19 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE


10903839 EMBASE No: 2000387570
Oral toleragens in rheumatoid arthritis
Choy E.H.S.
E.H.S. Choy, Guy's, King's/St. Thomas' Hosp., School of Medicine, King's College Hospital, East Dulwich Grove, London SE22 8PT United Kingdom
AUTHOR EMAIL: ernest.choy@kcl.ac.uk
Current Opinion in Investigational Drugs ( CURR. OPIN. INVEST. DRUGS ) ( United Kingdom) 2000, 1/1 (58-62)
CODEN: CIDRE ISSN: 0967-8298
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 52

Rheumatoid arthritis (RA) is a common inflammatory and destructive arthropathy. Its precise pathogenesis remains unknown but there is evidence to suggest it is an autoimmune disease. Recently, a number of candidate autoantigens have been identified in RA. Modulating the immune response to the autoantigens by oral tolerance may lead to safer and more effective treatment. Oral tolerance is a state of systematic immune suppression to an antigen induced by oral feeding of the same antigen. In animal models, oral feeding with pathogenic antigens prevents and reduces the severity of autoimmune diseases. Even in diseases where the pathogenic autoantigens are unknown, bystander suppression can be induced using antigens present in the anatomical vicinity. Hence, oral tolerance has been advocated as a treatment strategy for autoimmune diseases including RA. Clinical trials of chicken and bovine type II collagen, a major constituent of articular cartilage, produced conflicting results in RA. This review examines the scientific basis of oral tolerance, discusses the apparent discrepancy in clinical trial results and looks at the future prospect.

12/7/20 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE


10701099 EMBASE No: 2000189191
The immunologic homunculus in rheumatoid arthritis

Blass S.; Engel J.-M.; Burmester G.-R.
Dr. S. Blass, Charite University Hospital, Rheumatology/Clinical Immunol. Dept., Tucholskystrasse 2, D-10117 Berlin Germany
Arthritis and Rheumatism ( ARTHRITIS RHEUM. ) (United States) 1999, 42/12 (2499-2506)
CODEN: ARHEA ISSN: 0004-3591
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 62

12/7/21 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


135091514 CA: 135(7)91514r PATENT
Peptides designed for the diagnosis and treatment of rheumatoid arthritis
INVENTOR(AUTHOR): Union, Ann; Moereels, Henri; Meheus, Lydie
LOCATION: Belg.
ASSIGNEE: Innogenetics N.V.
PATENT: PCT International ; WO 200146222 A2 DATE: 20010628
APPLICATION: WO 2000EP13037 (20001220) *EP 99870280 (19991221) *EP 2000870195 (20000908)
PAGES: 53 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-007/08A
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG ; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
SECTION:
CA215002 Immunochemistry
CA209XXX Biochemical Methods
CA263XXX Pharmaceuticals
IDENTIFIERS: autoimmune disease rheumatoid arthritis citrulline peptide
DESCRIPTORS:
Diagnosis...
agents; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Antibodies...
anti-idiotypic; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Antibodies...
autoantibodies; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Antigens...
autoantigens; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Antibodies... Antigens... Autoimmune disease... Blood serum... Filaggrin... Immune tolerance... Peptides,biological studies... Protein sequences... Rheumatoid arthritis...
citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Peptides,biological studies...
cyclic; citrulline-contg. peptides for diagnosis and treatment of

rheumatoid arthritis
Test kits...
diagnostic; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Diagnosis...
immunodiagnosis; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Drug delivery systems...
immunotoxins; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Antibodies...
monoclonal; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Drug delivery systems...
nasal; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Diagnosis...
serodiagnosis; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
Membranes,nonbiological...
strip solid support; citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
CAS REGISTRY NUMBERS:
58-85-5 372-75-8 75536-80-0 347871-56-1P 347871-73-2P 347871-78-7P 347872-77-9P 347873-22-7P 347873-68-1P 347873-98-7P 347874-24-2P 347874-53-7P 347874-78-6P 347875-05-2P 347875-19-8P
citrulline-contg. peptides for diagnosis and treatment of rheumatoid arthritis
347875-37-0 347875-54-1 347875-70-1 347875-88-1 unclaimed sequence; peptides designed for the diagnosis and treatment of rheumatoid arthritis

12/7/22 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


134095494 CA: 134(8)95494m PATENT
Citrulline-containing fibrin derivatives, and their use for diagnosing or treating rheumatoid arthritis
INVENTOR(AUTHOR): Serre, Guy; Sebbag, Mireille
LOCATION: Fr.
ASSIGNEE: Universite Paul Sabatier - Toulouse III
PATENT: PCT International ; WO 0102437 A1 DATE: 20010111
APPLICATION: WO 2000FR1857 (20000630) *FR 998470 (19990701)
PAGES: 26 pp. CODEN: PIXXD2 LANGUAGE: French CLASS: C07K-014/75A; A61K-038/36B; A61P-019/02B; G01N-033/53B DESIGNATED COUNTRIES: CA; JP; US
DESIGNATED REGIONAL: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA201007 Pharmacology
CA215XXX Immunochemistry
IDENTIFIERS: fibrin citrulline deriv rheumatoid arthritis treatment, diagnosis rheumatoid arthritis fibrin citrulline deriv
DESCRIPTORS:
Fibrinogens...
and deiminated fibrinogen; citrulline-contg. fibrin derivs., and use

for diagnosing or treating rheumatoid arthritis
Filaggrin...
autoantibodies to; citrulline-contg. fibrin derivs., and use for diagnosing or treating rheumatoid arthritis
Antibodies...
autoantibodies; citrulline-contg. fibrin derivs., and use for diagnosing or treating rheumatoid arthritis
Antirheumatic agents... Fibrins... Immunoassay...
Proteins,general,biological studies... Rheumatoid arthritis... Test kits...
citrulline-contg. fibrin derivs., and use for diagnosing or treating rheumatoid arthritis
Proteins,specific or class...
conjugates, with carrier mols.; citrulline-contg. fibrin derivs., and use for diagnosing or treating rheumatoid arthritis
Animal tissue...
synovial; citrulline-contg. fibrin derivs., and use for diagnosing or treating rheumatoid arthritis
CAS REGISTRY NUMBERS:
372-75-8 2489-13-6 47295-77-2 99235-09-3 318500-71-9 318500-76-4
318500-81-1 citrulline-contg. fibrin derivs., and use for diagnosing or treating rheumatoid arthritis

12/7/23 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


Applicant

132011629 CA: 132(2)11629g PATENT
Peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of rheumatoid arthritis patients and their use in diagnosis
INVENTOR(AUTHOR): Serre, Guy Bruno Rene; Girbal Neuhauser, Elisabeth; Vincent, Christian; Simon, Michel; Sebbag, Mireille; Dalbon, Pascal; Jolivet Reynaud, Colette; Arnaud, Michel; Jolivet, Michel
LOCATION: Fr.
ASSIGNEE: Bio Merieux S. A.
PATENT: France Demande ; FR 2773157 A1 DATE: 19990702
APPLICATION: FR 9716673 (19971230)
PAGES: 21 pp. CODEN: FRXXBL LANGUAGE: French CLASS: C07K-014/47A; A61K-038/17B; G01N-033/564B
SECTION:
CA215002 Immunochemistry
IDENTIFIERS: rheumatoid arthritis diagnosis immunoassay autoantibody filaggrin epitope citrulline
DESCRIPTORS:
Antibodies...
autoantibodies; peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of rheumatoid arthritis patients and their use in diagnosis
Epitopes... Filaggrin... Immunoassay... Rheumatoid arthritis...
peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of rheumatoid arthritis patients and their use in diagnosis
CAS REGISTRY NUMBERS:
204391-63-9 204391-64-0 peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of rheumatoid arthritis patients and their use in diagnosis
251365-12-5 residues 71-119 of human filaggrin; peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of

rheumatoid arthritis patients and their use in diagnosis
225682-08-6 225682-09-7 unclaimed nucleotide sequence; peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of rheumatoid arthritis patients and their use in diagnosis
250722-30-6 unclaimed protein sequence; peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of rheumatoid arthritis patients and their use in diagnosis

12/7/24 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


132000444 CA: 132(1)444s PATENT
Use of filaggrin-derived citrulline-containing peptides for treatment of rheumatoid polyarthritis
INVENTOR(AUTHOR): Serre, Guy Bruno Rene; Girbal Neuhauser, Elisabeth; Vincent, Christian; Sebbag, Mireille; Simon, Michel; Dalbon, Pascal; Jolivet Reynaud, Colette; Arnaud, Michel; Jolivet, Michel
LOCATION: Fr.
ASSIGNEE: Universite Paul Sabatier Toulouse III
PATENT: France Demande ; FR 2773078 A1 DATE: 19990702
APPLICATION: FR 9716672 (19971230)
PAGES: 25 pp. CODEN: FRXXBL LANGUAGE: French CLASS: A61K-038/17A
SECTION:
CA201007 Pharmacology
CA215XXX Immunochemistry
IDENTIFIERS: citrulline contg filaggrin peptide rheumatoid polyarthritis
DESCRIPTORS:
Antibodies...
autoantibodies, to filaggrin; filaggrin-derived citrulline-contg. peptides for treatment of rheumatoid polyarthritis
Antirheumatic agents... Filaggrin... Peptides,biological studies...
filaggrin-derived citrulline-contg. peptides for treatment of rheumatoid polyarthritis
Lymphocyte...
plasma cell, synovial; filaggrin-derived citrulline-contg. peptides for treatment of rheumatoid polyarthritis
CAS REGISTRY NUMBERS:
372-75-8 arginine replacement by; filaggrin-derived citrulline-contg. peptides for treatment of rheumatoid polyarthritis
250686-73-8D 250686-74-9D 251102-69-9D arginine-to-citrulline replacement derivs., filaggrin-derived citrulline-contg. peptides for treatment of rheumatoid polyarthritis
74-79-3 biological studies, citrulline replacement for; filaggrin-derived citrulline-contg. peptides for treatment of rheumatoid polyarthritis
250686-75-0 filaggrin-derived citrulline-contg. peptides for treatment of rheumatoid polyarthritis

12/7/25 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


131031040 CA: 131(3)31040r PATENT
Synthetic peptides containing citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment

INVENTOR(AUTHOR): Meheus, Lydie; Union, Ann; Raymackers, Joseph
LOCATION: Belg.
ASSIGNEE: Innogenetics N.V.
PATENT: PCT International ; WO 9928344 A2 DATE: 19990610
APPLICATION: WO 98EP7714 (19981130) *EP 97870195 (19971128) *EP 98870078 (19980409)
PAGES: 74 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/47A; C07K-001/107B; C07K-016/18B; A61K-038/17B; G01N-033/564B
DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE ; LS; MW; SD; SZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
SECTION:
CA215002 Immunochemistry
CA203XXX Biochemical Genetics
IDENTIFIERS: filaggrin intermediate filament protein vimentin cytokeratin , autoantigen autoantibody rheumatoid arthritis autoimmune disease, antibody antiidiotype immunotoxin autoimmune disease tolerance
DESCRIPTORS:
Antibodies...
anti-idiotypic; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Antibodies...
autoantibodies; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Antigens...
autoantigens; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Peptides,biological studies...
citrulline-contg.; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Toxins...
conjugates, citrulline-contg. peptide; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Peptides,biological studies...
cyclic, citrulline-contg.; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Test kits...
diagnostic; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Lupus erythematosus...
discoid; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Immunoassay...
enzyme-linked immunosorbent assay; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Bacteria(Eubacteria)... Eukaryote(Eukaryotae)... Yeast...
host; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Drug delivery systems...

immunotoxins; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Proteins,specific or class...
intermediate filament-assocd.; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Antibodies...
monoclonal; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Gene...
regulatory; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Connective tissue...
scleroderma; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Membranes,nonbiological...
strip; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Autoimmune disease... Baculoviridae... Bioassay... Blood serum... Dermatomyositis... Drug screening... Filaggrin... Immune tolerance... Immunoassay... Molecular cloning... Protein sequences... Rheumatoid arthritis... Sjogren's syndrome... Vaccines... Vimentins...
synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Immune complexes...
synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera for increasing size and clearance of immune complexes in rheumatoid arthritis sera
Lupus erythematosus...
systemic; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Repetitive DNA...
tandem; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Medical goods...
test strip; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Keratins...
1; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
Keratins...
9; synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment
CAS REGISTRY NUMBERS:
372-75-8 75536-80-0 226904-10-5 226904-13-8 226904-18-3 226904-22-9 226904-27-4 226904-31-0 226904-37-6 226904-43-4 synthetic peptides contg. citrulline recognized by rheumatoid arthritis sera as tools for diagnosis and treatment

12/7/26 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)


128229350 CA: 128(19)229350y PATENT
Citrulline-containing antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis

INVENTOR(AUTHOR): Serre, Guy; Girbal-Neuhauser, Elisabeth; Vincent, Christian; Simon, Michel; Sebbag, Mireille; Dalbon, Pascal; Jolivet-Reynaud, Colette; Arnaud, Michel; Jolivet, Michel
LOCATION: Fr.
ASSIGNEE: Biomerieux; Serre, Guy; Girbal-Neuhauser, Elisabeth; Vincent, Christian; Simon, Michel; Sebbag, Mireille; Dalbon, Pascal; Jolivet-Reynaud, Colette; Arnaud, Michel; Jolivet, Michel
PATENT: PCT International ; WO 9808946 A1 DATE: 19980305
APPLICATION: WO 97FR1541 (19970901) *FR 9610651 (19960830)
PAGES: 37 pp. CODEN: PIXXD2 LANGUAGE: French CLASS: C12N-015/12A; C12N-001/21B; C07K-014/47B; C12N-009/78B; G01N-033/53B
DESIGNATED COUNTRIES: CA; US DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES ; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA215002 Immunochemistry
IDENTIFIERS: filaggrin citrulline diagnosis rheumatoid polyarthritis
DESCRIPTORS:
Antigens...
artificial; citrulline-contg. antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis
Diagnosis... Filaggrin... Rheumatoid arthritis...
citrulline-contg. antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis
Autoantibodies...
to filaggrin; citrulline-contg. antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis
CAS REGISTRY NUMBERS:
372-75-8 204391-63-9P 204391-64-0P 204594-23-0P citrulline-contg. antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis

12/7/27 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI


012601349
dates
WPI Acc No: 1999-407453/199935
Peptide containing epitope recognized by anti - filaggrin antibodies , used as immunoassay reagents for diagnosis of rheumatoid polyarthritis
Patent Assignee: BIO MERIEUX (INMR ); BIOMERIEUX SA (INMR )
Inventor: ARNAUD M; DALBON P; GIRBAL-NEUHAUSER E; JOLIVET M; JOLIVET-REYNAUD C; SEBBAG M; SERRE G; SIMON M; VINCENT C; GIRBAL N E; JOLIVET R C; SERRE G B R
Number of Countries: 077 Number of Patents: 004
Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week | |
|---|---|---|---|---|---|---|---|
| FR 2773157 | A1 | 19990702 | FR 9716673 | A | 19971230 | 199935 | B |
| WO 9935167 | A1 | 19990715 | WO 98FR2899 | A | 19981229 | 199935 | |
| AU 9919717 | A | 19990726 | AU 9919717 | A | 19981229 | 199952 | |
| EP 1042366 | A1 | 20001011 | EP 98964536 | A | 19981229 | 200052 | |
| | | | WO 98FR2899 | A | 19981229 | | |

Priority Applications (No Type Date): FR 9716673 A 19971230
Patent Details:

| Patent No | Kind | Lan | Pg | Main IPC | Filing Notes |
|---|---|---|---|---|---|
| FR 2773157 | A1 | | 21 | C07K-014/47 | |

WO 9935167 A1 F C07K-014/47
Designated States (National): AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KG KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
AU 9919717 A C07K-014/47 Based on patent WO 9935167
EP 1042366 A1 F C07K-014/47 Based on patent WO 9935167
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

Abstract (Basic): FR 2773157 A1
NOVELTY - Peptide (I) contains an epitope, recognized by anti - filaggrin antibodies (Ab) present in the serum of patients with rheumatoid polyarthritis (RP), comprises a tripeptide motif centered on a citrulline (Cit) residue present in at least one of three peptides of 49, 14 and 14 amino acids (sequences reproduced; fragments of filaggrin ).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) artificial antigen (AAg), recognized specifically by Ab, containing, or consisting of, at least one (I);
(2) antigenic composition for diagnosis of RP containing at least one (I) or AAg, optionally labeled or conjugated to a carrier molecule; and
(3) kits for detecting Ab containing (I) or AAg, plus suitable buffers and reagents.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - (I) are used as antigen for in vitro detection of Ab, for diagnosis of RP, in standard immunoassays.
ADVANTAGE - Ab are markers of RP and their detection makes possible diagnosis at an early stage.
pp; 21 DwgNo 0/0
Derwent Class: B04; S03
International Patent Class (Main): C07K-014/47
International Patent Class (Additional): A61K-038/17; G01N-033/53; G01N-033/564

12/7/28 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI


012601322
WPI Acc No: 1999-407426/199935
Filaggrin -derived citrulline peptide antigens, useful for treatment of rheumatoid arthritis
Patent Assignee: UNIV TOULOUSE SABATIER PAUL (UYTO-N)
Inventor: ARNAUD M; DALBON P; GIRBAL-NEUHAUSER E; JOLIVET M; JOLIVET-REYNAUD C; SEBBAG M; SERRE G; SIMON M; VINCENT C; GIRBAL N E; JOLIVET R C; SERRE G B R
Number of Countries: 077 Number of Patents: 005
Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week | |
|---|---|---|---|---|---|---|---|
| FR 2773078 | A1 | 19990702 | FR 9716672 | A | 19971230 | 199935 | B |
| WO 9934819 | A2 | 19990715 | WO 98FR2900 | A | 19981229 | 199935 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| AU 9919718 | A | 19990726 | AU 9919718 | A | 19981229 | 199952 |
| EP 1041997 | A2 | 20001011 | EP 98964537 | A | 19981229 | 200052 |
| | | | WO 98FR2900 | A | 19981229 | |
| JP 2002500195 | W | 20020108 | WO 98FR2900 | A | 19981229 | 200206 |
| | | | JP 2000527267 | A | 19981229 | |

Priority Applications (No Type Date): FR 9716672 A 19971230
Patent Details:

| Patent No | Kind | Lan | Pg | Main IPC | Filing Notes |
|---|---|---|---|---|---|
| FR 2773078 | A1 | | 26 | A61K-038/17 | |
| WO 9934819 | A2 | E | 26 | A61K-038/17 | |

Designated States (National): AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KG KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

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|---|---|---|---|---|
| AU 9919718 | A | | A61K-038/17 | Based on patent WO 9934819 |
| EP 1041997 | A2 | F | A61K-038/17 | Based on patent WO 9934819 |

Designated States (Regional): AT BE CH DE DK ES FI FR GB IE IT LI NL SE

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|---|---|---|---|---|
| JP 2002500195 | W | 27 | A61K-038/00 | Based on patent WO 9934819 |

Abstract (Basic): FR 2773078 A1

NOVELTY - Filaggrin -derived citrulline peptide antigens are new.

DETAILED DESCRIPTION - An antigenic peptide, specifically recognized by anti - filaggrin autoantibodies present in the serum of patients suffering from rheumatoid arthritis , constitutes a peptide derived from all or part of the sequence of a filaggrin unit. At least one arginine residue is substituted for citrulline . The peptide is used to obtain medicines to inhibit the autoantibodies from binding their antigenic target.

An INDEPENDENT CLAIM is also included for a pharmaceutical composition for the treatment of rheumatoid arthritis characterized in that it contains as main agent at least one antigenic peptide as above.

ACTIVITY - Anti-arthritic.

MECHANISM OF ACTION - Anti-Filiggrin AutoAntibody Inhibitor.

USE - The antigenic peptide is used to obtain medicines to inhibit anti-filiggrin autoantibodies from binding their antigenic target. Pharmaceutical compositions containing the citrulline peptides are used for the treatment of rheumatoid arthritis . All claimed.

ADVANTAGE - For in vivo administration and use of the antigenic peptides, the amino acids can be changed to the L-forms (especially to increase protease resistance) as well as undergo other modifications to enhance their life in cells.

pp; 26 DwgNo 0/3

Derwent Class: B04
International Patent Class (Main): A61K-038/00; A61K-038/17
International Patent Class (Additional): C07K-014/47; C07K-014-47; C07K-016/18; C12N-015/09

12/7/29 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI


012579250

WPI Acc No: 1999-385357/199932
New peptide derived from intermediate filament proteins
Patent Assignee: INNOGENETICS NV (INNO-N)
Inventor: MEHEUS L; RAYMACKERS J; UNION A
Number of Countries: 084 Number of Patents: 005
Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week | |
|---|---|---|---|---|---|---|---|
| WO 9928344 | A2 | 19990610 | WO 98EP7714 | A | 19981130 | 199932 | B |
| AU 9921558 | A | 19990616 | AU 9921558 | A | 19981130 | 199945 | |
| EP 949270 | A1 | 19991013 | EP 98870078 | A | 19980409 | 199947 | |
| EP 1034186 | A2 | 20000913 | EP 98965715 | A | 19981130 | 200046 | |
| | | | WO 98EP7714 | A | 19981130 | | |
| HU 200004338 | A2 | 20010228 | WO 98EP7714 | A | 19981130 | 200121 | |
| | | | HU 20004338 | A | 19981130 | | |

Priority Applications (No Type Date): EP 98870078 A 19980409; EP 97870195 A 19971128
Patent Details:

| Patent No | Kind | Lan | Pg | Main IPC | Filing Notes |
|---|---|---|---|---|---|
| WO 9928344 | A2 | E | 73 | C07K-014/47 | |

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

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|---|---|---|---|---|
| AU 9921558 | A | | C07K-014/47 | Based on patent WO 9928344 |
| EP 949270 | A1 | E | C07K-014/47 | |

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

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|---|---|---|---|---|
| EP 1034186 | A2 | E | C07K-014/47 | Based on patent WO 9928344 |

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

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|---|---|---|---|---|
| HU 200004338 | A2 | | C07K-014/47 | Based on patent WO 9928344 |

Abstract (Basic): WO 9928344 A2

NOVELTY - (A) A novel peptide comprises a sequence of less than 50 amino acids of any variant of natural filaggrin or any variant of intermediate filament proteins is new.

DETAILED DESCRIPTION - (A) A novel peptide comprises a sequence of less than 50 amino acids of any variant of natural filaggrin or any variant of intermediate filament proteins, comprising at least one citrulline residue, and where the presence of the citrulline is crucial for reacting with antibodies that are present in sera from patients with rheumatoid arthritis (RA).

INDEPENDENT CLAIMS are also included for the following:

(1) an antibody specifically reactive with the citrulline residues of a peptide form as in (A) or specifically reactive with the citrulline residues of intermediate filament proteins, and with the antibody being preferably a monoclonal antibody (MAb);

(2) anti-idiotype antibody raised upon immunization with an antibody as in (1), with the anti-idiotype antibody being specifically reactive with an antibody as in (1), to mimic the peptide that contains citrulline as in (A), and with the antibody being preferably an MAb;

(3) an immunotoxin molecule comprising and/or consisting of cell recognition molecule being a peptide as in (A), or an antibody as in

(1), to mimic the peptide that contains citrulline as in (A), and with the antibody being preferably a MAb;

(4) use of intermediate filament protein, preferably vimentin or cytokeratin 1 or cytokeratin 9, or antibodies raised upon immunization with intermediate filament proteins or a composition for the preparation of a therapeutic or of a diagnostic for RA;

(5) a diagnostic kit for use in detecting auto-immune diseases such as RA, systemic lupus erythematosus, discoid lupus erythematosus, scleroderma, dermatomyositis and Sjogren's syndrome, the kit comprising at least one peptide as in (A), or an antibody as in (1), or an intermediate filament protein, with the peptide, antibody or protein being optionally bound to a solid filament.

USE - The peptides constitute immunogenic determinants of antibodies present in patients with RA. The peptides, antibodies , immunotoxins and intermediate filament proteins can be used for the preparation of a therapeutic or of a diagnostic for RA (claimed). The peptides can also be used for identifying compounds which modulate the interaction between an autoantigen and a RA specific autoantibody . The products can also be used for the diagnosis and treatment of other autoimmune diseases e.g. systemic lupus erythematosus, discoid lupus erythematosus, scleroderma, dermatomyositis, or Sjogrens syndrome.

pp; 73 DwgNo 0/7

Derwent Class: B04; D16; S03

International Patent Class (Main): C07K-014/47

International Patent Class (Additional): A61K-038/17; C07K-001/107; C07K-016/18; G01N-033/564

12/7/30 (Item 4 from file: 351)

DIALOG(R)File 351:Derwent WPI



011790132

WPI Acc No: 1998-207042/199818

Artificial antigen recognised by anti - filaggrin auto - antibodies - is modified form of filaggrin with citrulline replacing at least one arginine, used for diagnosis of rheumatoid polyarthritis

Patent Assignee: BIOMERIEUX SA (INMR )

Inventor: ARNAUD M; DALBON P; GIRBAL-NEUHAUSER E; JOLIVET M; JOLIVET-REYNAUD C; SEBBAG M; SERRE G; SIMON M; VINCENT C; GIRBAL NEUHAUSER E; JOLIVET R C

Number of Countries: 020 Number of Patents: 003

Patent Family:

| Patent No | Kind | Date | Applicat No | Kind | Date | Week | |
|---|---|---|---|---|---|---|---|
| WO 9808946 | A1 | 19980305 | WO 97FR1541 | A | 19970901 | 199818 | B |
| FR 2752842 | A1 | 19980306 | FR 9610651 | A | 19960830 | 199818 | |
| EP 929669 | A1 | 19990721 | EP 97938965 | A | 19970901 | 199933 | |
| | | | WO 97FR1541 | A | 19970901 | | |

Priority Applications (No Type Date): FR 9610651 A 19960830

Patent Details:

| Patent No | Kind | Lan | Pg | Main IPC | Filing Notes |
|---|---|---|---|---|---|
| WO 9808946 | A1 | F | 36 | C12N-015/12 | |

Designated States (National): CA US

Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

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|---|---|---|---|---|---|
| EP 929669 | A1 | F | | C12N-015/12 | Based on patent WO 9808946 |

Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE

FR 2752842 A1 C07K-014/78

Abstract (Basic): WO 9808946 A

Artificial antigen (Ag) recognised specifically by anti - filaggrin autoantibodies (Ab) present in the serum of patients with rheumatoid polyarthritis (RPA) is a recombinant or synthetic polypeptide containing at least part of a sequence derived from a filaggrin unit, or related molecule, by substitution of at least 1 arginine residue by citrulline (Cit).

USE - Ag are used for in vitro diagnosis of RPA from complex formation with Ab in usual immunoassays.

ADVANTAGE - Replacement of Arg by Cit is essential for antigen-specific recognition by Ab.

Dwg.0/5

Derwent Class: B04; D16; S03

International Patent Class (Main): C07K-014/78; C12N-015/12

International Patent Class (Additional): C07K-014/47; C12N-001/21; C12N-009/78; G01N-033/53; G01N-033/532; G01N-033/564; G01N-033/68

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